The overarching theme of this issue of the ILAR Journal is the neural control of social behavior. In the introduction, Scott Wersinger observes that animal behavior is diverse both across species and among members of the same species, but that there are common characteristics that define social behaviors. Based on his insights and those of the other articles in this issue, I identify challenges and opportunities that institutional animal care and use committees (IACUCs) face when evaluating animal study protocols that involve the analysis and measurement of animal behavior.

Why might behavioral studies pose unique challenges for IACUCs? As explained below, the reasons are as diverse as the behavior itself. But, in addition, behavioral assessment plays a role when the primary goal of the study is not the assessment of behavior; for example, the Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research (NRC 2003, 23) discuss behavioral assessment as a tool for determining animal well-being:

Animal behavior can be an excellent measure for assessing overall health, indeed, the clinical signs used to diagnose disease in animals are often based on behavior (for example, signs of pain). A sound understanding of animal behavior is key for the veterinarian or other professional in assessing animal health.

“Other” professionals obviously include the members of the IACUC and, in this instance, their “sound understanding” of species-specific animal behavior. IACUCs must therefore evaluate not only the science of animal use protocols but also how investigators will use behavior to assess animal welfare.

The common thread among the articles in this issue is that familiarity in this context doesn’t breed contempt but rather leads to good animal welfare. Investigators and IACUC members have an ethical and moral obligation to ensure that animals in behavioral experiments experience a minimum of pain and distress. Yet IACUCs often make evaluations with scant knowledge of species-specific needs and concerns. The Guide for the Care and Use of Laboratory Animals (NRC 1996, 10) suggests that, when a protocol includes procedures that are unfamiliar to IACUC members, “relevant objective information should be sought from the literature, veterinarians, investigators, and others knowledgeable about the effects on animals.” I discuss this in more detail below.

Challenges

Understanding Normal Behavior

Because the generalizability of behavioral results depends on knowledge of “normal” behavior, and experimental results are often compared to it, the articles in this issue reinforce the need for investigators, IACUC members, veterinarians, and caretakers to understand such behavior. IACUCs may see measurements of normal and experimental social behavior and endocrinology in the same protocol, and these assessments may trigger concerns about the health and well-being of individual animals. In her article on the “Neuroendocrinology of Social Behavior” Elizabeth Adkins-Regan describes various neuroendocrine mechanisms, the social consequences of infusing neuroendocrine-affecting substances (e.g., hormones, dopamine, corticosteroids) into the CNS, and common ways of studying these consequences.

Determining Risk versus Benefit

In “The Neurobiology of Sexual Reward,” Raúl G. Paredes mentions behavioral studies in which animals must overcome aversive stimuli to reach desired goals. Such studies are particularly challenging, especially if the aversive stimuli inflict pain, and require IACUCs to, in a sense, do a risk-benefit analysis. If the “goal” to be reached by the experimental animal is a tethered or restrained conspecific, the IACUC evaluation becomes more complex because the committee must consider the welfare of both the subject and the restrained animal. The myriad details of behavioral studies are sometimes lost on those not familiar with specific experimental

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1Abbreviation used in this article: IACUC, institutional animal care and use committee

2For a categorization of the signs of pain in laboratory animals, see NRC (2003, 17); animal distress is the subject of the recent ILAR report on Recognition and Alleviation of Distress in Laboratory Animals (NRC 2008).
approaches. This is true for most IACUC reviewers unless
the committee is lucky enough to have a member knowl-
dgeable in the subdiscipline.

Seeking Expert Opinion

It makes sense for the IACUC to consider scents when evalu-
ating protocols. From the article on “Olfactory Regulation of
the Sexual Behavior and Reproductive Physiology of the Lab-
oratory Mouse: Effects and Neural Mechanisms” by Kevin
R. Kelliher and Scott R. Wersinger, it is reasonable to conclude
that (1) an “expert” in the idiosyncratic behavior of mice should
be on the IACUC, (2) the committee should be aware of poten-
tial experimental pitfalls from olfactory effects (more on this
below), and (3) facilities managers should be well versed in
the effects of chemosensory cues on sexual behavior and should
adjust room assignments and ventilation accordingly.

Understanding Communication

In “Communication of Adult Rats by Ultrasonic Voca-
lation: Biological, Sociobiological, and Neuroscience Ap-
proaches,” Stefan M. Brudzynski examines behaviors that
are unheard of by some IACUCs, whose members may not
appreciate that rat vocalizations are in the ultrasonic range
and thus are inaudible to caregivers and investigators alike.
Rats make such vocalizations during stress, distress, and
danger. IACUCs should take this into consideration when
approving areas for behavioral testing, perioperative proce-
dures, and euthanasia. Keeping rats aurally isolated from
other rodents in situations that may cause anxiety is humane
and obviously the right thing to do.

Appreciating Patterned Behavior

Behavior often occurs in complex and predictable patterns,
as in maternal behavior, but may be extremely species spe-
cific, so generalization without direct observation may lead
to erroneous expectations about health and well-being. In-
vestigators and IACUC members alike should therefore ap-
preciate subtle aspects of patterned behaviors. In “The
Biopsychology of Maternal Behavior in Nonhuman Mammals,”
Mark B. Kristal reminds us that a behavior pattern may actually be “a smoothly coordinated constellation of
simpler actions with proximate causes that, when sequenced
properly, have the appearance of a motivated, purposive,
adaptive pattern of caretaking.” To the extent that this ob-
servation applies to other behaviors deemed normal for a stud-
ied species, distress or stress, pain or suffering may alter
parts of any behavioral constellation, and the effect of even
small alterations on the whole may be profound or masked
by the complexity of the behaviors themselves. Kristal cau-
tions researchers to be diligent in deconstructing complex
behaviors and analyzing components. IACUC members
should be similarly cautious.

Being Selectively Anthropomorphic

It is usually good advice to guard against anthromor-
phism, but there is at least one useful exception to this ad-
vise. The Public Health Service Policy on Humane Care
and Use of Laboratory Animals (NIH 2002) requires the in-
stitutional official to ensure adherence to nine principles,
two of which are germane to IACUC evaluation of behavior
as a welfare indicator. Principle IV states that, “Unless the
contrary is established, investigators should consider that
procedures that cause pain or distress in human beings may
cause pain and distress in other animals.” And according to
Principle VII, “The living conditions of animals should be
appropriate for their species and contribute to their health
and comfort.” These statements reinforce the need for all
personnel involved to appreciate the special needs and con-
cerns associated not only with each species but also with
individual members of that species. The development of
such appreciation depends on knowledge and experience,
and to this end Principle VIII states that “Investigators and
other personnel shall be appropriately qualified and experi-
enced for conducting procedures on living animals. Ade-
quate arrangements shall be made for their in-service
training, including the proper and humane care and use of
laboratory animals.” If “other personnel” include those who
evaluate study proposals then it is clear that IACUC mem-
ers must be trained properly, and this training should in-
clude the behavior of the species used in the study proposals
they evaluate.

Deliberately Designing Spaces

IACUCs are responsible for ensuring that the design of ani-
mal facilities and laboratories allows the normal and com-
plete expression of an animal’s behavioral repertoire. In
“Optimization of Laboratory Conditions for the Study of
Social Behavior,” Scott R. Wersinger and Lisa B. Martin
note that “social behavior is particularly sensitive to envi-
ronmental factors that are affected by routine animal hus-
dandry”; if social behavior is used to assess animal
well-being then the sensitivities mentioned above (e.g.,
scents, ultrasonic vocalizations) will influence observers’
perceptions of animal well-being. Space requirements for,
sanitation of, behavior apparatuses are sometimes over-
looked by those tasked with determining their adequacy and
efficacy. Because of group housing, animals usually express
behaviors in the presence of other conspecifics, and normal
husbandry may have negative effects both on their social
behavior and on behavior used to gauge well-being. The au-
thors suggest that “Investigators new to the analysis of so-
cial behavior often fail to appreciate the minute details that
can have profound effects on behavior”; might this not hold
as well for IACUC members? This article serves as a primer
for investigators who study social behavior and for IACUC
members who consider protocols that involve animal
behavior.
Allowing Freedom of Expression

IACUCs face a number of challenges in determining, before studies commence, the best way to balance animal welfare and animal science involving behavior, and they must understand and appreciate many aspects of experimental and housing environments. Behavioral testing requires special chambers, special environmental controls, extra space (sometimes away from housing areas), and special sanitation procedures. With the increasing use of barrier facilities, alternatively, behavioral testing apparatus may be brought to the animals rather than having animals go to the testing facilities. But without an explicit rationale indicating the contrary, facilities will provide standard care based on their knowledge of species-specific best practices, and IACUC members will evaluate animal use protocols based on what knowledge they have about the animals, the work, and standard welfare practices.

An animal’s behavioral expression is influenced by, and influences, other animals in the holding and testing areas. For example, rodents may produce ultrasonic vocalizations of high intensity in the presence of stressors and, as Brudzynski explains, these “sounds” may elicit responses in other animals in the vicinity. Thus, when evaluating procedures and sites for rodent euthanasia, it is essential to consider ultrasonic exposure. Similarly, predator scents may be unintentionally and inappropriately introduced into animal rooms by fomites and cause distress that, as Wersinger and Martin point out, if unrelied may be considered USDA category E by some IACUCs. In addition, if behavior is a criterion to assess an animal’s well-being, the animal should be observed during the appropriate part of its activity cycle: nocturnal, diurnal, and crepuscular species each present unique challenges for observers. It is therefore crucial to bear in mind that animals thought to be exhibiting “normal” physiology and pharmacological reactions just before tissue harvesting may actually not be. IACUC members may rightly question animal welfare under these conditions.

Furthermore, in many instances individual behavioral profiles must be kept separate because behavioral responses vary among individuals of the same species. The need to identify individual animals in groups creates challenges during behavioral experiments because tests often are carried out over multiple sessions. Permanent identification has traditionally involved altering the physical appearance of individuals for the sake of convenience, but that convenience must be balanced with animal welfare. With the advent of new tracking technologies (such as microchips) IACUCs may suggest that tagging methods be refined, thus giving a new avenue for the application of the principles of the 3Rs (see, e.g., ILAR Journal 43(3), Advanced Physiological Monitoring in Rodents).

Enrichment practices present other behavioral challenges to IACUCs when assessing the experimental environment but they are beyond the scope of consideration here (readers may wish to consult ILAR Journal 46(2), Enrichment Strategies for Laboratory Animals).

Opportunities

Opportunities created by the challenges mentioned above lead to what we might call “the 3Bs” of IACUC behavior. IACUCs must consider basics, blend, and balance in their efforts to ensure on the part of an institution, and to reassure the community, that investigators engage in the responsible use of animals in testing, research, and education.

Basics

Evaluation of animal use protocols that describe new or unusual procedures, activities, or conditions affords an IACUC the chance to take stock of the expertise available among its members and to assess the “basics” of the institution’s resources, procedures, and balance of expertise to determine what additional resources are necessary to conduct an effective protocol review. Semianual program reviews provide scheduled opportunities to do this, but unique protocols give IACUCs opportunities for midcourse reflections and corrections.

IACUCs that are unfamiliar with some aspect of a proposed animal study have several options. They may consider using ad hoc reviewers who have specialty expertise (see Silverman et al. 2007, 57-58, §§ 5:50-5:52). If consultants with needed expertise are not readily available, IACUC members may consider approving pilot studies as a means of gaining familiarity. Pilot studies are particularly useful for determining the appropriate number of animals needed (see, e.g., Silverman et al. 2007, 184, § 13:9). They also provide investigators, IACUC members, veterinarians, and animal caretakers with opportunities to become familiar with specific behaviors, conditions, and outcomes on a limited scale before committing fully to a novel procedure or protocol.

Blend

The next step is to incorporate, or “blend,” the information from expert consultants and pilot studies into the IACUC’s thinking and acting. If real estate involves “location, location, location,” optimal IACUC behavior involves “education, education, education.” When an IACUC lacks the necessary expertise to evaluate protocols it must seek increased training for its members to ensure their familiarity with the nuances of unusual studies and species. The investigators who proposed the study may be the best source of such training, which may simply be a formal dialogue as part of the protocol review process. Investigators also need to understand what IACUCs look for when reviewing protocols so that they can provide clear and concise descriptions that facilitate evaluation and reduce review time. IACUCs can train investigators on the “what, how, and when” of an effective protocol by providing them with two distinct opportunities for teachable moments: during the prereview process and at IACUC meetings. Dialogue breeds understanding that extends far beyond a single protocol review because similar issues are bound to arise. After all, behavioral studies rarely
are done in isolation; rather, a study may have one or more unique variants but incorporate approaches common to others at that institution.

Balance

IACUCs need to balance what seems to be good with what is actually good both for the animals and for the experiments. An animal’s behavior in the laboratory may differ from its behavior in the wild, so baselines must be situationally specific. Adaptation of husbandry schedules to the animals’ needs rather than the caretaker’s convenience can improve animal welfare. For example, it may be appropriate to honor an investigator’s request to lengthen the time between cage changes or to do so only when measured ammonia levels reach threshold. Anecdotes—for example, about birds rearing their young better in wooden boxes rather than in clean cages—may also suggest variations. These insights and exceptions underscore the need to balance species requirements with prescriptions based on engineering standards derived from what, at one time, were best practices.

Summary

If extended far enough, appreciation of species-specific needs and concerns can be a form of enrichment. A team approach to enrichment is based on understanding and action (Nelson and Mandrell 2005). The enrichment team—the investigators, IACUC members, veterinary staff, and caretakers—should have an understanding of the animals’ needs and preferences, and apply best practices in enrichment in a thoughtful and well-reasoned way, balancing the needs of the animal with the scientific goals of the experiments in which the animals play a crucial part.

References


